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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,223	03/02/2004	Mel H. Epstein	3474.1001-011	3953

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
06/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/791,223	EPSTEIN ET AL.	
	Examiner	Art Unit	
	Brian-Yong S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-17, 19, 26-27, 30-33 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,20-25,28,29 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03/02/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/08/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicant's filing of amendment/remarks on 02/08/2008. By the amendment, claims 18, 26, 28, 29, 30 and 31 have been amended. Claims 18, 20-25, 28, 29 and 34 are currently pending for prosecution on the merits of the application.

2. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 18, 20-25 and 28-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims in this application introduce new limitation to the claimed invention, namely "any methamphetamine". The examiner determines that when all evidences in the original disclosure are considered and carefully reviewed, the newly amended claims fail to find support in the original specification.

The term "any methamphetamine" allows for the inclusion of not only enantiomer of methamphetamine such as l-methamphetamine and d-methamphetamine, but also (±) methamphetamine, salt, derivative, analogs and precursors thereof, etc…

The specification discloses that the invention relates to the discovery that a particular enantiomer of amphetamine such as l-amphetamine or levo-amphetamine or methamphetamine such as l-methamphetamine or levo-amphetamine is effective for treating the instant claimed condition (i.e., Alzheimer's disease). As the specific embodiment, about 51 percent, about 60 percent, about 75 percent, about 80 percent, about 85 percent, about percent 95 percent or about 99 percent of one amphetamine enantiomer relative to another amphetamine enantiomer or one methamphetamine enantiomer relative to another methamphetamine enantiomer, namely 1-amphetamine relative to d-amphetamine or 1-methamphetamine relative to d-methamphetamine.

Therefore, it would have been clear to one skilled in the art, reading the instant disclosure, that the claimed invention can be practiced with a composition predominantly comprises of l-amphetamine and/or 1-methamphetamine, substantially free of d-amphetamine or d-methamphetamine.

As discussed above, the specification only supports for "a methamphetamine" as l-methamphetamine and d-amphetamine. There is no express statement about the genus of "any methamphetamine" that can be found in the specification. Thus, the amendment that renders the claims broader than the original disclosure raises the issue of lack of written description under the first paragraph of 35 USC 112.

Suggest rewording of "the step of administering an effective amount of an amphetamine to the human, wherein the amphetamine is administered as a component of a composition that

includes amphetamine and any methamphetamine, wherein at least about 85 mole percent of the total amphetamine and methamphetamine…" in claim 18 to " the step of administering an effective amount of a composition that includes at least one member selected from the group consisting of l-amphetamine and l-methamphetamine to the human having Alzheimer's disease, wherein the l-amphetamine is at least about 85 mole percent l-amphetamine relative to the total l-amphetamine and l-methamphetamine content of the composition". Similar claim amendments are suggested in claims 26, 28 and 29.

4. Claims 18, 20-25 and 28-29 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses l-methamphetamine or d-methamphetamine as the suitable example of methamphetamine which meets the written description and enablement provisions of 35 USC 112, first paragraph. However, the claims 18, 20-25 and 28-29 are directed to encompass "any methamphetamine" which only corresponds in some undefined way to specifically instantly disclosed chemicals. None of these meet the written description provision of 35 USC 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompasses a myriad of possibilities. To the extent that no structure function data is disclosed in connection with theses functionally described compounds to correlate, or there is not disclosed correlation established between these functional drugs and the contemplated desired therapeutic effect to be achieved in practicing the

instant invention, the specification provides insufficient written description to support the genus encompassed by the claims.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of 1-methamphetamine or d-methamphetamine enantiomer, the skilled artisan cannot envision the detailed chemical structure of the encompassed derivatives, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565,*

1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 18, 20-25, 28-29 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Filip et al. (Reference No. C74: "Selegiline in the Treatment of Alzheimer's Disease: a Long-Term Randomized Placebo-Controlled Trial", J. Psychiatry Neurosci 1999, Vol 24, No. 3, pp. 234-43) in view of Gelowitz et al. (Reference No. C82: "Chronic L-Deprenyl or L-Amphetamine: Equal Cognitive Enhancement, Unequal MAO Inhibition", Pharmacology Biochemistry and Behavior, Vo. 47, pp. 41-15, 1994), and further in view of Yasar et al. (Reference No. C257: "Are Metabolite of L-Deprenyl (Selegiline) Useful or Harmful? Indications from Preclinical Research", J Neural Transm Suppl 1996, 48:61-73).

Filip teaches a use of selegiline (l-deprenyl) for the treatment of Alzheimer's disease.

Gelowitz teaches that l-deprenyl is evaluated and known to be useful in improving the cognitive and reducing the behavioral alterations of Alzheimer's disease (page 41, column 1, 1st paragraph to bridging paragraph in column 2); that selegiline is metabolized into mainly l-(-)-methamphetamine and l-(-)-amphetamine in the liver and the cognitive and locomotor effects of l-deprenyl reflect the action of its amphetamine metabolites rather than its own MAO-B inhibitor (page 41, column 2, paragraph 2 to bridging paragraph in page 42); and that l-amphetamine is as effective as l-deprenyl in enhancing the cognitive performance (page 44, column 1, lines 6-15).

Yasar is being provided as a supplemental reference to demonstrate the state of art knowledge in potential benefit of using l-stereoisomers of l-amphetamine and/or l-methamphetamine over d-isomer counterparts in enhancing cognitive function and of providing clinical actions as comparable to l-deprenyl ("Discussion" in page 70-71, particularly, page 70, first paragraph; page 71, last paragraph).

The teaching of Filip differs from the claimed invention in the use of composition comprising amphetamine and methamphetamine wherein said composition is delivered essentially in l-amphetamine in "at least about 85 mole percent", "at least about 95 mole percent" or "at a dose of at least about 2mg and 60 mg dose per day".

To incorporate such teaching into the teaching of Filip, would have been obvious in view of Gelowitz who teaches or suggests the activity of metabolites of l-deprenyl (i.e., l-amphetamine and l-methamphetamine) in enhancing the cognitive performance of Alzheimer's disease and Yasar who teaches the potential advantage of using l-stereoisomers of l-amphetamine and/or l-methamphetamine in enhancing cognitive function over d-isomer counterparts which is known to be associated with the excessive stimulation of behavior characteristics and signs of neurotoxicity.

One having ordinary skill in the art would have expected as taught by Gelowitz and Yasar that metabolites of l-deprenyl (i.e., l-amphetamine and 1-methamphetamine), particularly l-amphetamine, would be effective as l-deprenyl in enhancing the cognitive performance of Alzheimer's patients. Thus, one having ordinary skill in the art would have motivated to select l-amphetamine and/or l-methamphetamine as active ingredients with expectation that l-amphetamine and/or l-methamphetamine would provide similar activity as l-deprenyl.

With respect to the specific molar percentage or dosage amounts of said compound, such determination of concentration or amounts is considered within the skill of artisan, and the artisan would be motivated to determine optimum concentration or dosage having maximum therapeutic index. Generally, differences in concentration or dosage amounts will not support the patentability of subject matter encompassed by the prior art there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller, 220 F. 2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).*

One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 18, 20-25, 28-29 and 34 are provisionally rejected under the judicially created doctrine of double patenting over claims 1, 4, 17, 21 and 23 of copending Application No.11/305495. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

Although the conflicting claims are not identical, they are not patentably distinct from each other because one having ordinary skill in the art would have known that the methamphetamine (l-methamphetamine) would be metabolized to amphetamine (l-amphetamine) in human body and would provide similar activity as the instantly claimed l-amphetamine in the treatment Alzheimer's disease. See Specification, page 20, lines 12-14 of the copending 11/305495 and Gilles et al., The Journal of Pharmacology and Experimental Therapeutics, Vol. 292. No. 3, pp. 1042-1047, 2000.

5. Claims 18, 20-25, 28-29 and 34 are rejected under the judicially created doctrine of double patenting over claims 1-23, 28-35 of U. S. Patent No. USP 7244769 or claims 1-28 of U.S. Patent No. 6828351.

Although the patented claims do not specifically identify the use of said l-amphetamine in the treatment of Alzheimer's disease, one having ordinary skill in the art, reading the entire specification (see for example USP'351, column 9, line 4-5, column 10, line 61, column 14, lines 57-58, column 19, lines 4-5, column 28, lines 58-59, column 48, line 10 and USP'769, column 12, line 27, column 14, lines 36-37, column 17, line 56, column 23, lines 65-66, column 29, lines 50-51, column 40, line 29, column 63, line 34), would have expected that l-amphetamine is useful for the treatment of Alzheimer's disease by improving in memory consolidation. Thus,

using the specification as "dictionary" in this ODP (obviousness-type double patenting) rejection analysis, the patented claims of US'769 and US'351 make obvious the instant invention.

With respect to the specific molar percentage or dosage amounts of said compound, particularly the instant "at least about 85 mole percent", "at least about 95 mole percent" or "at a dose of at least about 2mg and 60 mg dose per day", such determination of concentration or amounts is considered within the skill of artisan especially in view of the overlapping molar percentages or dosage amounts disclosed in the copending applications, and the artisan would be motivated to determine optimum concentration or dosage having maximum therapeutic index. Generally, differences in concentration or dosage amounts will not support the patentability of subject matter encompassed by the prior art there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller, 220 F. 2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).*

Conclusion

7. No Claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614